



(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention  
of the grant of the patent:  
**19.12.2001 Bulletin 2001/51**

(51) Int Cl.7: **A61K 7/20, A61K 7/16**

(21) Application number: **92308294.5**

(22) Date of filing: **11.09.1992**

(54) **Abrasive tooth whitening dentifrice of improved stability**

**Abrasive Zahnpasta zur Bleichung von Zähnen mit verbesserter Haltbarkeit**

**Dentifrice abrasif pour le blanchiment des dents ayant une stabilité améliorée**

(84) Designated Contracting States:  
**AT BE CH DE DK ES FR GB IE IT LI LU NL SE**

(30) Priority: **13.09.1991 US 759241**  
**13.09.1991 US 759244**

(43) Date of publication of application:  
**07.04.1993 Bulletin 1993/14**

(73) Proprietor: **Colgate-Palmolive Company**  
**New York, N.Y. 10022-7499 (US)**

(72) Inventors:  
• **Nathoo, Salim A.**  
**Piscataway, New Jersey (US)**  
• **Prencipe, Michael**  
**East Windsor, New Jersey (US)**

• **Chmielewski, Mary Beth**  
**Piscataway, New Jersey (US)**  
• **Drago, Vincent**  
**Staten Island, New York (US)**  
• **Smith, Sahar Fakhry**  
**Bordentown, New Jersey (US)**

(74) Representative:  
**Kearney, Kevin David Nicholas et al**  
**KILBURN & STRODE 20 Red Lion Street**  
**London, WC1R 4PJ (GB)**

(56) References cited:  
**EP-A- 0 325 267 WO-A-88/06879**  
**WO-A-93/00884 FR-A- 1 559 617**  
**US-A- 4 592 487 US-A- 4 988 500**

**EP 0 535 816 B1**

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

## D scripti n

[0001] This invention relates generally to preparations for whitening human teeth, and more particularly, to a stable, storable composition which when applied onto the surface of teeth acts to whiten and polish teeth without damage to oral tissues.

The Prior Art

[0002] A tooth is comprised of an inner dentin layer and an outer hard enamel layer that is the protective layer of the tooth. The enamel layer of a tooth is naturally an opaque white or slightly off-white color. It is this enamel layer that can become stained or discolored. The enamel layer of a tooth is composed of hydroxyapatite mineral crystals that create a somewhat porous surface. It is believed that this porous nature of the enamel layer is what allows staining agents and discoloring substances to permeate the enamel and discolor the tooth.

[0003] Many substances that a person confronts or comes in contact with on a daily basis can "stain" or reduce the "whiteness" of one's teeth. In particular, the foods, tobacco products and fluids such as tea and coffee that one consumes tend to stain one's teeth. These products or substances tend to accumulate on the enamel layer of the tooth and form a pellicle film over the teeth. These staining and discoloring substances can then permeate the enamel layer. This problem occurs gradually over many years, but imparts a noticeable discoloration of the enamel of one's teeth.

[0004] Dentifrices, especially toothpaste, gels and powders containing active oxygen or hydrogen peroxide liberating ingredients such as peroxides, percarbonates and perborates of the alkali and alkaline earth metals or complex compounds containing hydrogen peroxide with salts of the alkali or alkaline earth metals have been disclosed in the prior art for the whitening of teeth. However, of all the peroxide compounds suggested by the prior art for whitening teeth, only two peroxide releasing compounds, urea peroxide and hydrogen peroxide, are approved by the Food and Drug Administration for use in oral compositions.

[0005] One method for whitening teeth used by dental professionals involves the use of 35% hydrogen peroxide in combination with heat and light to promote the oxidation reaction. This method, although fast, is losing favor with dentists because clinical and scientific evidence shows that high concentrations of peroxide are deleterious to oral tissues.

[0006] Another professional method for whitening teeth involves the use of hydrogen peroxide generating compounds such as urea peroxide (carbamide peroxide) at concentrations of about 10% to achieve the desired whitening effect. Urea peroxide rapidly breaks down into hydrogen peroxide due to the water present in saliva. This method is known as an office-monitored at-home bleaching system and involves the use of a mouth guard or tray within which the bleaching agent is placed. The tray is then placed upon the teeth of the patient and bleaching is allowed to take place. This method of treatment has drawbacks including tooth sensitivity, possibly due to demineralization and irritation of oral tissues. An additional disadvantage of the tray application method is that the bleaching effect is very slow.

[0007] There is a demand in the marketplace for a tooth whitening product that can be used at home or in private by the consumer and is safe and easy to use. A product for home use cannot utilize the compositions or products for whitening teeth that are available for use by a trained dental professional. For example, the 35% hydrogen peroxide bleaching agent utilized by many dental practitioners to bleach teeth is sufficiently concentrated to be irritating and potentially dangerous for home use by the consumer.

[0008] There are available in the marketplace non-abrasive dentifrice compositions for home use which contain 1-3% by weight concentrations of hydrogen peroxide and when brushed on the teeth effect whitening and removal of stains.

[0009] A drawback to the use of home use bleaching dentifrices containing oxygen liberating bleaching compounds is the tendency of these products to decompose within a relatively short period of time following manufacture with concomitant loss of all or a substantial amount of the available oxygen thereby limiting the efficacy of these products as teeth whitening compositions. Peroxy compounds such as hydrogen peroxide are notoriously unstable with respect to maintenance of peroxide level and have been found to be difficult to formulate into aqueous gels or pastes which will have an adequate shelf-life and yet will readily liberate oxygen when applied to the oral cavity. Therefore, the prior art, for example U.S. 4,988,450 and U.S. 3,657,413 in formulating oxygen liberating compositions for the whitening of teeth utilize anhydrous powders or water-free pastes or gels which must be protected against contamination and chemical interaction. A drawback to the use of such anhydrous products is that, due to the absence of water, application of the oral composition tends to desiccate oral tissues which leads to irritation and tissue damage.

[0010] Dentifrice whitening products formulated with peroxy compounds normally do not contain abrasive polishing agents as such materials activate the rapid decomposition of the peroxy compounds whereby the oxygen whitening agent is prematurely released. The gas evolution is especially undesirable with a toothpaste or gel product as such gas evolution can cause swelling and/or bursting of tubes containing same. Capped tubes filled with dentifrice products containing peroxy compounds and silica abrasives have been known to explode within one day after filling. When alumina abrasives are substituted for silica, the filled product is pocketed with gas bubbles within days of filling.

[0011] A drawback to the use of whitening products which are formulated without abrasives is that, in addition to having a slow bleaching action, the products are not effective in stain removal. Thus the polishing agent incorporated in a dentifrice acts to debride and physically scrub the external surface of teeth. This scrubbing action removes filmy bacterial and plaque layers as well as some of the stains and discoloring pigments that are found on teeth that cause the undesired discoloration. These polishing agents also microabrade the tooth so as to polish the teeth to give the enamel a more lustrous appearance and a higher optical sheen. This microabrasion action enhances the scrubbed teeth's ability to reflect white light and thereby appear brighter.

[0012] Illustrative of non-abrasive oral compositions containing peroxide compounds include U.S. 4,980,152; 4,839,156; 4,522,805 and 4,567,036.

[0013] U. S. 4,980,152 discloses a non-abrasive aqueous oral gel composition comprising about 0.5 to about 10% by weight urea peroxide and 0.01 to 2% by weight of a fluoride providing compound. The composition further includes a thickening agent such as carboxy polymethylene, a non-ionic surfactant such as Pluronic F127, alkali soluble cellulose ethers as viscosity increasing agents, potassium phosphate as a buffering agent and glycerine as a carrier and flavoring and sweetening agents.

[0014] U.S. Patent Nos. 4,839,156 discloses an aqueous dental gel containing 18-25% by weight of a polyoxyethylene polypropylene block copolymer gelling agent, hydrogen peroxide, flavor, sweetening agent and a non-ionic surfactant as the essential ingredients.

[0015] U.S. Patent Nos. 4,522,805 and 4,567,036 disclose a stable toothpaste to aid in controlling periodontal disease, containing an oxidizing agent such as carbamide peroxide (urea peroxide) which dissociates into urea and hydrogen peroxide in the oral cavity, in a paste carrier comprising an anionic detergent, sorbitol and glycerin humectant and a thickening agent such as gum tragacanth, sodium alginate or sodium carboxymethyl cellulose.

[0016] U.S. Pat. No. 4,405,599 discloses a toothpaste consisting essentially of a combination of calcium peroxide and sodium perborate oxidizing agents, dicalcium phosphate dihydrate, calcium carbonate and magnesium carbonate cleaning agents, sorbitol humectant, cornstarch and cellulose gum thickening agents, and an anionic detergent.

EP-A-325267 discloses a dentifrice comprising 10% hydrogen peroxide (35% solution) and 29% calcium pyrophosphate. The hydrogen peroxide is prepared using deionised water.

FR-A-1559617 discloses a dentifrice comprising 2% urea peroxide and 20% dicalcium phosphate.

WO-A-8806879 discloses a dentifrice comprising 3.9% urea peroxide and 10% dicalcium phosphate.

WO-A-9300884 (cited under Art 54(3)EPC) discloses a dentifrice comprising 2% of hydrogen peroxide solution stabilised with colloidal silver, and 36% of dicalcium phosphate. None of these disclose the subject matter of the present invention.

#### Summary of the Invention

[0017] According to the present invention there is provided the non therapeutical use of an aqueous abrasive oral composition of a dicalcium phosphate compound, a metal ion free peroxide, a chelating agent and a thickening agent for whitening of teeth. The metal ion free peroxide may be urea peroxide or hydrogen peroxide.

[0018] The composition preferably comprises 5 - 30%, preferably 15 to 25%, by weight of water. It may contain 20 - 30% by weight of a dicalcium phosphate abrasive, 1 to 20% by weight of a metal ion free peroxide, 0.1 to 8.0% by weight of a chelating agent and 1.0 to 20% by weight of a thickening agent. The chelating agent may be disodium calcium ethylene diamine tetracetic acid or phosphoric acid.

[0019] As will hereinafter be illustrated, the dentifrice compositions of the present invention exhibit better peroxide efficacy in removing stains from teeth than previously attained by the prior art. The compositions are stable at elevated temperatures, and can be used for both office monitored at-home applications as well as private brushing applications.

#### DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0020] The term "dicalcium phosphate compound" as used herein includes within its meaning both dicalcium phosphate-dihydrate and anhydrous dicalcium phosphate or calcium pyrophosphate. Dicalcium phosphate-dihydrate and calcium pyrophosphate are compounds which have long been used as cleaning agents in toothpastes. These calcium phosphate compounds have remineralizing properties, their ionic constituents are practically the same as those contained in dental enamel, which they combine with the property of imparting excellent cleaning and polishing effects to oral compositions made therefrom. A high beta phase calcium pyrophosphate is preferred as the dicalcium phosphate compound for use in the present invention.

[0021] The dentifrice compositions are formulated using a metal ion free peroxide compound as the whitening agent, a dicalcium phosphate compound as the abrasive polishing agent, a humectant, a surfactant, a sweetener and flavor.

[0022] The dentifrice compositions are further formulated using as ingredients, a metal ion free peroxide compound as the whitening agent, a dicalcium phosphate compound as the abrasive polishing agent chelating agents such as

sodium ethylene diamine tetracetic acid and sodium acid pyrophosphate, a thickening agent such as a poly (ethylene oxide) resin or a polyoxyethylene polyoxypropylene block copolymer thickener.

[0023] Examples of suitable metal ion free peroxide compounds used to prepare the oral compositions include hydrogen peroxide and organic peroxides including urea peroxide (percarbamide), glyceryl peroxide, benzoyl peroxide and the like. A preferred organic peroxide is urea peroxide.

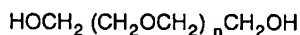
[0024] The peroxide component of the composition is included in an amount sufficient to allow release of sufficient oxygen when the composition is contacted with water, e.g., during brushing of teeth, to effect whitening thereof. Typically, the peroxide can be employed in the composition in amounts so that at least about 1% of the composition comprises a peroxide. Preferably, the peroxide comprises from about 1 to about 20% by weight of the composition. More preferably, the peroxide comprises from about 5 to about 20% by weight of the composition. The active peroxide content (i.e., the equivalent of  $H_2O_2$  in the peroxide employed) is preferably between about 0.5 and about 6% by weight, and more preferably between about 1 and about 3% by weight.

[0025] The presence of a dicalcium phosphate compound in the composition in addition to its polishing function has been found to provide significant increased peroxide stability of the compositions in comparison to compositions with other abrasives. For example, when 40% by weight of calcium pyrophosphate was employed in combination with 10% by weight urea peroxide in a polyethylene glycol carrier, a 95% residual peroxide level was found after storage of the composition in a closed container for 14 days at elevated temperatures (e.g. 100°F (38°C)).

[0026] In preparing the dentifrice compositions, the dicalcium phosphate compound is included in the composition in an amount effective so as to inhibit breakdown of the peroxide in the composition during storage in a closed container, but so as to allow release of sufficient oxygen from the peroxide when the composition is contacted with water, e.g., during brushing of teeth, to effect whitening thereof. Typically, the dicalcium phosphate compound is included in the composition in an amount of from 20 to about 60% by weight, preferably from about 35 to about 55%.

[0027] Glycerin, sorbitol and polyethylene glycol in combination with water are useful as carrier materials in the composition. A combination of polyethylene glycol and water is preferred as the carrier.

[0028] Illustrative of the polyethylene glycols useful in the practice of the present invention include polyethylene glycols known by the trademark CARBOWAX which are nonionic polymers of ethylene oxide having the general formula:



wherein n represents the average number of oxyethylene groups. The Carbowax polyethylene glycols are designated by a number such as 400, 600, 800, etc. which represents the average molecular weight. The average molecular weight of the polyethylene glycols used herein is about 200-1000, preferably 400-800 and most preferably 600 (PEG 600).

[0029] The glycerine, sorbitol or polyethylene glycol is included in the compositions in an amount of from about 2 to about 20% by weight and preferably about 5 to about 15% by weight. Water is incorporated in the aqueous dentifrice compositions at a concentration of about 5 to about 30% by weight of the composition and preferably about 15 to about 25% by weight.

[0030] A surfactant is also included in the dentifrice composition and serves as a solubilizing, dispersing, emulsifying and wetting agent and is especially effective in solubilizing the flavor present. A particularly useful surfactant is a nonionic water soluble polyoxyethylene monoester of sorbitol with a  $C_{10-18}$  fatty acid ester of sorbitol (and sorbitol anhydrides), consisting predominantly of the monoester, condensed with about 10-30, preferably about 20, moles of ethyleneoxide. The fatty acid (aliphatic hydrocarbon-monocarboxylic acid) may be saturated or unsaturated, e.g. lauric, palmitic, stearic, oleic acids. Tween 20 is especially preferred, which is a polyoxyethylene (20) sorbitan monolaurate. The nonionic surfactant may constitute about 0.5 to 5.0% by weight and preferably 0.5 to 3% by weight of the oral composition.

[0031] Other classes of surfactants such as cationic surfactants, anionic surfactants such as sodium laurylsulfate and sodium laurylsulfoacetate, ampholytic or amphoteric surfactants like cocoamidopropyl betaine can also be employed.

[0032] Other useful surfactants include anionic surfactants such as water soluble salts of higher fatty acid monoglyceride monosulfates, such as sodium salts of the monosulfated monoglycerides, or hydrogenated coconut oil fatty acids, higher alkylsulfates, such as sodium lauryl sulfate and alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate. Sodium lauryl sulfate is especially preferred as a surfactant in compositions containing urea peroxide.

[0033] The flavor ingredient constitutes about 0.5 - 5.0% by weight of the dentifrice composition. Suitable flavoring constituents are flavoring oils, e.g., oils of spearmint, peppermint, wintergreen, sassafras, clove, sage, eucalyptus, marjoram, cinnamon, ethyl acetate, methyl salicylate, and menthol.

[0034] A sweetening material is preferably also employed as a complement to the flavoring material. Suitable sweetening agents are water soluble and include sodium saccharin, sodium cyclamate, xylitol, aspartame and the like, in concentrations of about 0.01 to 1.0% by weight. Sodium saccharin is preferred.

**[0035]** Thickening or gelling agents are also used in the formulation of the dentifrice. Thickening agents include natural and synthetic gums and gum-like materials, such as carrageenan, Xanthan gum, alkali metal (e.g., K, Na) carboxymethyl cellulose and hydroxymethyl carboxymethyl cellulose, polyvinyl pyrrolidone, water soluble hydrophilic colloidal carboxyvinyl polymers such as those sold under the trademark Carbopol 934 and 940, hydroxyethyl cellulose, India gum, locust bean gum, agar, modified starches, inorganic thickeners such as colloidal silica, e.g. synthetic finely-divided silica including those sold under the trademarks Cab-O-Sil Syloid, and Aerosil, or cross-linked polycarboxylate polymers available from GAF under the designation Gantrez ACV series. The thickening and gelling agents are preferably present in the dentifrice in an amount within the range of about 0.3 to about 6% by weight.

**[0036]** Particularly useful thickening agents included in the composition are polyoxyethylene polyoxypropylene block copolymers and poly(ethylene oxide) resins in amounts from about 10% to about 25% by weight of the composition. Illustrative of the polyoxyethylene polyoxypropylene block copolymers useful in the practice of the present invention include block copolymers having the formula  $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b\text{H}$  wherein a is an integer such that the hydrophobic base represented by  $(\text{C}_3\text{H}_6\text{O})_b$  has a molecular weight of about 2750 to 4000, b is an integer such that the hydrophilic portion (moiety) represented by  $(\text{C}_2\text{H}_4\text{O})_a$  constitutes about 70-80% by weight of the copolymer. Block copolymers of this composition are available commercially under the trademark Pluronic F type.

**[0037]** Pluronic F127, which has a molecular weight of 4000 and contains 70% of the hydrophilic polyoxyethylene moiety is preferred in the practice of the present invention.

**[0038]** Poly (ethylene oxide) resinous thickeners are available commercially in a molecular weight range of 50,000 to 5,000,000.

**[0039]** Polyoxy N-10 available from Union Carbide Corp. as granules of water soluble poly (ethylene oxide) pseudo-plastic resin having a molecular weight of about 100,000 and a Brookfield viscosity of 44 CPS (25°C, spindle 1, speed 50 rpm) is a preferred poly(ethylene oxide) pseudoplastic resin thickener for use in the dentifrice compositions.

**[0040]** Other pseudoplastic resins such as acrylic acid polymers and cellulose esters may also be used as thickeners in the whitening compositions.

**[0041]** The thickening agents are preferably present in the dentifrice in an amount within the range of about 1.0 to about 20 percent by weight and about 3 to about 10 percent by weight is preferred for use in the dentifrice compositions.

**[0042]** Fluorine-providing salts having anti-caries efficacy may also be incorporated in the dentifrice and are characterized by their ability to release fluoride ions in water. Among these materials are inorganic metal salts, for example, sodium fluoride, potassium fluoride, cuprous fluoride, a tin fluoride such as stannous fluoride or stannous chlorofluoride, sodium fluorosilicate, ammonium fluorosilicate, sodium monofluorophosphate, alumina mono- and di-fluorophosphate.

**[0043]** It is preferable to employ a fluoride compound to release about 10-1,500 ppm of fluoride ion.

**[0044]** Pyrophosphate salts having anti-tartar efficacy such as a dialkali or tetra-alkali metal pyrophosphate salts such as  $\text{Na}_4\text{P}_2\text{O}_7$ ,  $\text{K}_4\text{P}_2\text{O}_7$ ,  $\text{Na}_2\text{K}_2\text{P}_2\text{O}_7$ ,  $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$  and  $\text{K}_2\text{H}_2\text{P}_2\text{O}_7$ , long chain polyphosphates such as sodium hexametaphosphate and cyclic phosphates such as sodium trimeta phosphate may be incorporated in the dentifrice products preferably at a concentration of about 0.5 to about 8.0% by weight.

**[0045]** Synthetic anionic linear polymeric polycarboxylates which may be employed in the form of their partially or preferably fully neutralized water soluble alkali metal (e.g. potassium and preferably sodium) or ammonium salts may also be incorporated in the dentifrice compositions. Preferred are 1:4 to 4:1 copolymers of maleic anhydride or acid and a polymerizable ethylenically unsaturated monomer, preferably a lower alkyl vinyl ether such as methoxyethylene, having a molecular weight of about 30,000 to about 1,000,000 available commercially from GAF Corporation under the trademark Gantrez. A preferred polycarboxylate for use in the present invention is Gantrez S-97 which has a molecular weight of 97,000. The polycarboxylate compounds are incorporated in the compositions at a concentration of about 0.1 to about 5% by weight and preferably about 0.3 to about 1.0 percent by weight.

**[0046]** The dentifrice product may also contain conventional additional ingredients such as coloring or whitening agents, or preservatives such as sodium benzoate, in minimal amounts of up to 5% by weight and preferably up to 1%, provided they do not interfere with the chemical and cosmetic (physical) stability properties of the finished product.

**[0047]** Peroxide stabilizers are also present in the composition, such as sequestering or chelating agents, buffers, acidulating agents, coating or encapsulating agents. Suitable chelating agents include sodium acid pyrophosphate, salts of ethylene diamine tetraacetic acid, e.g., disodium calcium ethylene diamine tetraacetic acid ( $\text{Na}_2\text{Ca EDTA}$ ), phosphoric acid, citric acid, sodium citrate, potassium citrate, sodium pyrophosphate, potassium pyrophosphate, disodium, ethylenediamine tetraacetate and other amino polycarboxylic acids. Other examples of suitable chelating agents are diethylene triamine pentaacetic acid, phosphonates such as Dequest (trademark) available from Monsanto Chemical Company and azacycloheptane 2,2' diphosphonate. Such chelating agents stabilize the peroxide containing compositions by chelating metal ions such as  $\text{Fe}^{+3}$ ,  $\text{Mn}^{+2}$  and  $\text{Cu}^{+2}$ . The chelating agents are incorporated in the dentifrice compositions in an amount within the range of 0.1 to about 8.0% by weight and preferably about 0.5 to about 6.0% by weight.

**[0048]** Acidulating agents can be any organic acids like acetic acid, citric acid, lactic acid or gluconic acid. The acidulating agents are incorporated in the compositions at concentrations of about 0.1 to about 6.0% by weight of the

composition.

[0049] Examples of suitable coating agents for encapsulating the peroxide include Carbowax, gelatin, and mineral oil.

[0050] Agents used to diminish teeth sensitivity such as strontium chloride, potassium nitrate and potassium citrate can also be included in the compositions at concentrations of about 0.1 to about 10% by weight.

5 [0051] In addition, anti-foaming agents such as simethicone may also be incorporated in the dentifrice compositions at a concentration of 0.001 to about 0.1% by weight of the composition.

[0052] In preparing the dentifrice compositions, it is advantageous to maintain the pH of the composition in a near neutral or slightly acidic range, e.g., about 5.0 to about 7.5.

10 [0053] The dentifrice composition may be prepared by suitably mixing the ingredients. For instance, a gelling agent such as carboxymethyl cellulose is dispersed with a humectant, water, polycarboxylate, peroxide compound, salts such as tetrasodium pyrophosphate, sodium acid pyrophosphate, sodium fluoride or sodium monofluoro-phosphate, and saccharin are then added and mixed. The dicalcium phosphate, surfactant, and flavor are then added. The ingredients are then mixed under vacuum for about 15-30 minutes. The resulting gel or paste is then tubed.

15 [0054] The following examples are further illustrative of the present invention, but it is understood that the invention is not limited thereto. All amounts and proportions referred to herein and in the appended claims are by weight unless otherwise indicated.

[0055] A series of toothpastes were prepared using the following ingredients:

Ingredients	COMPOSITION NO.				
	1 %	2 %	3 %	4 %	C %
Urea Peroxide	10	10	10	---	---
H <sub>2</sub> O <sub>2</sub>	---	---	---	3.0	3.0
25 Calcium Pyrophosphate	40	40	40	40	---
Glycerine	q.s. to 100	q.s. to 100	---	---	-
PEG-600	5	5	q.s. to 100	q.s. to 100	15
PEG-8000	---	---	8	---	---
30 CMC	1.3	1.3	---	---	---
Cab-o-sil	---	---	---	4	---
Gantrez S-97 (solids)	1.73	1.73	---	---	---
35 Na <sub>4</sub> P <sub>2</sub> O <sub>7</sub>	2	2	---	0.3	---
Na <sub>2</sub> H <sub>2</sub> P <sub>2</sub> O <sub>7</sub>	---	---	---	1.7	---
NaF	---	25ppm	---	---	---
40 Flavor	1.5	1.5	1.5	1.5	1.5
Tween 20	1.2	1.2	1.2	1.2	1.2
DI H <sub>2</sub> O (deionized water)	9.8	9.8	---	7.0	q.s. to 100
Pluronic F-127	---	---	---	---	20.0
45 Saccharin	---	---	---	---	0.2

50 [0056] Composition 1 was prepared by mixing glycerine, PEG 600 (polyethylene glycol 600) together with CMC (carboxymethyl cellulose), then adding Gantrez S-97, urea peroxide, Na<sub>2</sub>H<sub>2</sub>P<sub>2</sub>O<sub>7</sub>, and Na<sub>4</sub>H<sub>2</sub>P<sub>2</sub>O<sub>7</sub>. The mixture was placed in a double planetary vacuum mixer. Calcium pyrophosphate, flavor and surfactant (Tween 20) were added to the mixture and the ingredients mixed under vacuum for about 15-20 minutes. A homogeneous paste was obtained.

[0057] Composition 2 was prepared in the same manner as Composition 1 except that 25 ppm NaF was included in the composition.

55 [0058] Composition 3 was prepared by heating PEG 600 to 130°F (54°C) adding PEG 8000 (polyethylene glycol 8000) and urea peroxide. The mixture is then transferred to a double planetary vacuum mixer. Calcium pyrophosphate was added and the resulting paste mixed for 5 minutes. Flavor and surfactant were added and then mixed for an additional 15 minutes under vacuum.

[0059] Composition 4 was prepared by adding fumed silica (Cab-o-Sil) to PEG-600. Water, urea peroxide, Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub>

and  $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$  were added and mixed until all the ingredients were well dispersed. To the resulting gel, calcium pyrophosphate, flavor oil and surfactant were added and mixed under vacuum for 15-20 minutes.

[0060] For comparative purposes, Composition C, a Pluronic gel formula containing 3%  $\text{H}_2\text{O}_2$ , was prepared following the procedure outlined in U.S. Patent No. 4,839,156.

[0061] Compositions 1-4 were tested for whitening efficacy. Extracted human molars having a high degree of discoloration were exposed for 6 hours at 37°C to Compositions 1-4 to determine the whiteness of the teeth.

[0062] Before the discolored teeth were exposed to Compositions 1-4, the color of the teeth was measured with a Gardner tristimulus colorimeter using values obtained from the CIE  $L^*$ ,  $a^*$  and  $b^*$  scale. This scale represents the mathematical approximation of the non-linear response of the eye to light.

[0063] A zero value for  $a^*$  and  $b^*$  means some shade of gray. Positive values for  $a^*$  and  $b^*$  indicate redness and yellowness. Negative  $a^*$  and  $b^*$  represents values for green and blue. After the 6 hour exposure time, the color of the teeth was again measured. The increase in whiteness is calculated using the equation  $\Delta E = \sqrt{(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2}$  where  $\Delta E$  represents an increase in whiteness.  $\Delta L^*$ ,  $\Delta a^*$  and  $\Delta b^*$  represent the changes that have occurred in these parameters after the bleaching process.

[0064] The  $\Delta E$  values are recorded in Table I. For purposes of comparison, the test procedure of Example I was repeated with the exception that comparative Composition C which did not contain calcium pyrophosphate was tested for whiteness. The results obtained with this comparative composition are also recorded in Table I below.

TABLE I

Increase in Whiteness	
Composition	Delta E
1	7.1
2	7.8
3	6.6
4	6.2
C	4.9

The data recorded in Table I show that when extracted human molars are exposed to compositions of the present invention which contain calcium pyrophosphate, they achieve an increase in whiteness which is on average 41% higher than teeth exposed to composition C, which does not contain calcium pyrophosphate abrasive.

## EXAMPLE II

[0065] The chemical stability of compositions 1,3 and 4 of Example I was determined by initially analyzing the compositions for active oxygen (AO) and then storing the composition for 2 week periods at elevated temperatures (100°F (38°C), 110°F (43°C)) and again analyzing the dentifrice for AO.

[0066] The results of these analyses are summarized in Table II below.

TABLE II

Composition Stability						
composition No.	pH	AO % Initial	AO % 2 wks @		AO % Recovery	
			100°F (38°C)	110°F (43°C)	100°F (38°C)	110°F (43°C)
1	5.5	1.65	1.55	---	94	---
1	6.0	1.65	1.42*	--	86	---
3	5.1	1.59	1.48	1.43	93	90
4	6.2	1.51	1.43	1.30	95	86

\* Results are after 3 weeks.

[0067] The data recorded in Table II indicate that the stability of the peroxide dentifrices of the present invention is greater than 90% after 2 weeks at 100°F (38°C) and greater than 86% after 2 weeks at 110°F (43°C) indicating that these oral compositions are relatively stable.

[0068] For purposes of comparison, a commercially available dentifrice sold as a tooth whitening composition was purchased at a local store. Ingredients listed on the product label included: water, sorbitol, dicalcium phosphate dihy-

drate, sodium bicarbonate, aluminum hydroxide, magnesium carbonate, calcium carbonate, cellulose gum, calcium peroxide and sodium perborate. When the dentifrice was analyzed for active oxygen, and it was determined that there was none, indicating low storage stability of the peroxy compounds included in the dentifrice.

### 5 EXAMPLE III

[0069] The stain removal properties of Composition 4 of Example I is recorded in Table III below. An additional composition of the present invention was prepared designated Composition 5 which was prepared in the same manner as Composition 1 of Example I, except that the thickening agent was Gantrez cross-linked with 1, 9 decadiene, designated Gantrez ACV-4006. The cross-linked Gantrez was substituted for CMC in Composition 1. Composition 5 also did not contain  $\text{Na}_4\text{P}_2\text{O}_7$  or  $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$  or Gantrez S-97.

[0070] The stain removal properties of the compositions 4 and 5 are recorded in Table III below. The data recorded in Table III shows the stain removal efficacy of toothpastes obtained from bovine teeth stained with tea and coffee after 50 strokes of brushing with compositions 4 and 5.

TABLE III

STAIN REMOVAL	
Composition No.	Delta E
4	13.0
5	11.5
C	2.9

[0071] The data recorded in Table III demonstrate that the compositions of the present invention effect superior stain removal, especially when compared to Composition C, thereby demonstrating the improved efficacy in stain removal attainable with the combination of a dicalcium phosphate abrasive compound and a peroxide compound.

### EXAMPLE IV

[0072] An aqueous, abrasive whitening paste was prepared using the following ingredients:

INGREDIENTS	%
Urea Peroxide	10.0
Calcium Pyrophosphate	27.5
Di Calcium phosphate dihydrate	5.0
Glycerine	4.995
PEG-600	10.0
Polyox N-10	5.0
Sodium lauryl Sulfate	0.2
$\text{Na}_2\text{Ca}$ EDTA	1.0
Simethicone	0.005
$\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$	2.0
Methyl Salicylate	0.75
DI $\text{H}_2\text{O}$	18.4
Pluronic F-127	15.0
Saccharin	0.1

[0073] The paste was prepared in a Ross mixer. Water, sodium acid pyrophosphate and Polyox N-10 were stirred for 30 minutes. Pluronic F-127 and Polyethylene Glycol 600 were added and the mixture stirred for 1.5 hours at a vacuum of -15 mmHg. Urea Peroxide was added to the mixture and stirring was continued for an additional 30 minutes at -15 mmHg vacuum. Simethicone, saccharin,  $\text{Na}_2\text{Ca}$  EDTA, sodium lauryl sulfate and flavor were added and mixed for 15 minutes without vacuum. Then, a vacuum of 30 mmHg was applied and stirring continued for an additional 30 minutes. Calcium Pyrophosphate was added and stirring was continued for 30 minutes under vacuum (-30mmHg). Dicalcium phosphate dihydrate and glycerine were added and mixed for a further 30 minutes under vacuum. The resulting product was a paste. The product when packaged in a tube was stable and could be stored without evidence



of peroxide decomposition.

[0074] To determine the whitening efficacy of the paste, three caries-free natural stained human molars were pumiced with Mytol (trademark) Tooth Cleaning Paste, and the initial color was determined by reflectance spectrometry using the Minolta Chroma Meter. The teeth were immersed in the paste prepared in Example IV and periodically removed and examined over a 4 hour period, and five readings of L, a and b were taken of each examined tooth.

[0075] The change in color was then calculated using the equation:

$$\Delta E = [(\Delta L^*)^2 + (\Delta a)^2 + (\Delta b^*)^2]^{1/2}$$

[0076] Where delta E represents an increase in whiteness. The higher the delta E value, the whiter the tooth, a delta E value of 14 being the most white and a delta E value of 1 being the least white or discolored. These values are based on the calibration of the Minolta chroma meter using the Trubyte Bioform (trademark) color ordered shade guide.

[0077] The delta E values are recorded in Table IV below.

[0078] For purposes of comparison, the procedure of Example IV was repeated with the exception that comparative Composition C which did not contain calcium pyrophosphate, or the chelating agents dicalcium sodium EDTA, phosphoric acid, and sodium acid pyrophosphate was also tested for whiteness. The results obtained with this comparative composition designated composition "C" are also recorded in Table IV below.

[0079] When the composition of Example IV was prepared without the chelating agents and the product tubed, bubbles rapidly formed in the product with the eventual bursting of the tube.

[0080] For purposes of further comparison, the procedure of Example IV was repeated with the exception that a professional tooth bleaching gel obtained from a dentist consisting of urea peroxide in an anhydrous glycerine base was also tested for whitening. The results obtained with this commercial product designated Composition "C<sub>1</sub>" are also recorded in Table IV.

TABLE IV

Increase in Whiteness			
Composition	Delta E		
	HOURS		
	1	2	4
EX. IV	5.5	6.4	8.1
C	2.4	3.4	4.7
C <sub>1</sub>	2.11	3.5	4.78

[0081] The delta E values recorded in Table IV show the increased whiteness of human molars obtained with an oral composition of the present invention, especially when compared with the comparative compositions C and C<sub>1</sub>.

#### EXAMPLE V

[0082] An aqueous, abrasive paste was prepared using the following ingredients:

INGREDIENTS	%
H <sub>2</sub> O <sub>2</sub> (35%)	10.0
Dicalcium phosphate di-hydrate	50.0
PEG-600	7.5
Phosphoric Acid	0.5
Na <sub>2</sub> CaEDTA	1.0
Methyl salicylate	0.75
Tween 20	0.60
DI H <sub>2</sub> O	19.55
Pluronic F-127	10.0
Saccharin	0.1

[0083] The ingredients were mixed together in a Ross mixer. In preparing the paste composition, a gel was first made

by mixing water, Polyethylene Glycol 600 and Pluronic F-127 for 1 hour under vacuum and then allowed to stand under vacuum for at least 1 hour. After a clear gel was formed, the 35% hydrogen peroxide solution and phosphoric acid were added to the resulting mixture and stirring was continued for another 1 hour period under vacuum. Sodium saccharin, disodium-calcium EDTA, Tween-20 and methyl salicylate were then added and the stirring was continued under vacuum for an additional 1 hour. Finally, dicalcium phosphate dihydrate was added and the mixture stirred under vacuum for 2 hours, and left overnight under vacuum. The resulting product was a paste.

[0084] The tooth whitening efficacy of the paste of Example V was tested using a Minolta Chroma Meter following the procedure of Example IV. The results are recorded in Table V.

[0085] For purposes of comparison, Composition C<sub>1</sub> was again tested for whitening efficacy. The results of this comparative test are also recorded in Table V.

[0086] When the composition of Example V was prepared without the chelating agents, phosphoric acid and Na<sub>2</sub>C<sub>4</sub> EDTA, and the product tubed, bubbles rapidly formed in the product with the eventual bursting of the tube.

TABLE V

Composition	Increase in Whiteness		
	Delta E Hours		
	1	2	4
EX. II	2.36	4.44	6.25
C <sub>1</sub>	2.11	3.50	4.78

[0087] The delta E values recorded in Table V show the increased whiteness of human molars obtained with the composition of the present invention, especially when compared with the comparative composition C<sub>1</sub>.

#### Claims

1. The non-therapeutical use of an aqueous abrasive oral composition of a dicalcium phosphate compound, a metal ion free peroxide, a chelating agent and a thickening agent for whitening of teeth.
2. The use as claimed in Claim 1 wherein the metal ion free peroxide is urea peroxide.
3. The use as claimed in Claim 1 wherein the metal ion free peroxide is hydrogen peroxide.
4. The use as claimed in Claim 1 wherein the composition contains 5 to 30% by weight of water.
5. The use as claimed in Claim 4 wherein the composition contains 15 to 25% by weight of water.
6. The use as claimed in any one of Claims 1 to 5 wherein the chelating agent is disodium calcium ethylene diamine tetraacetic acid.
7. The use as claimed in any one of Claims 1 to 5 wherein the chelating agent is phosphoric acid.

#### Patentansprüche

1. Nicht-therapeutische Verwendung einer wässrigen abreibenden oral anwendbaren Zusammensetzung aus Dicalciumphosphatverbindung, metallionenfreiem Peroxid, Chelatbildner und Verdickungsmittel zum Weißmachen von Zähnen.
2. Verwendung nach Anspruch 1, bei der das metallionenfreie Peroxid Hamstoffperoxid ist.
3. Verwendung nach Anspruch 1, bei der das metallionenfreie Peroxid Wasserstoffperoxid ist.
4. Verwendung nach Anspruch 1, bei der die Zusammensetzung 5 bis 30 Gew.% Wasser enthält.
5. Verwendung nach Anspruch 4, bei der die Zusammensetzung 15 bis 25 Gew.% Wasser enthält.

## EP 0 535 816 B1

6. Verwendung nach einem der Ansprüche 1 bis 5, bei der der Chelatbildner Dinatriumcalciummethylen-diamintetraessigsäure ist.

7. Verwendung nach einem der Ansprüche 1 bis 5, bei der der Chelatbildner Phosphorsäure ist.

5

### Revendications

1. Utilisation non thérapeutique d'une composition orale abrasive aqueuse d'un composé de phosphate dicalcique, un peroxyde dépourvu d'ion métallique, un agent chélatant et un agent épaississant pour le blanchiment des dents.

10

2. Utilisation selon la revendication 1, dans laquelle le peroxyde dépourvu d'ion métallique est le peroxyde d'urée.

3. Utilisation selon la revendication 1, dans laquelle le peroxyde dépourvu d'ion métallique est le peroxyde d'hydrogène.

15

4. Utilisation selon la revendication 1, dans laquelle la composition contient de 5 à 30 % en poids d'eau.

5. Utilisation selon la revendication 4, dans laquelle la composition contient de 15 à 25 % en poids d'eau.

20

6. Utilisation selon l'une des revendications 1 à 5, dans laquelle l'agent chélatant est le calcium disodique de l'acide éthylène-diamino-tétraacétique.

7. Utilisation selon l'une des revendications 1 à 5, dans laquelle l'agent chélatant est l'acide phosphorique.

25

30

35

40

45

50

55